REMARKS

The Office Action dated April 28, 2005 has been carefully reviewed. Claims 1 and 4-8 are pending in the application. Claims 2-3, 9-12, and 295-300 have been canceled. Claims 13-294 have been withdrawn without prejudice to the right to file one or more divisional applications. Applicant requests reconsideration of the rejection and allowance of the claims on the basis of the following remarks.

Summary of Examiner Interview

Applicant thanks the Examiner for the courtesies extended during the telephone interview conducted on July 15, 2005.

With respect to Claim 1, the Examiner indicated that the 35 USC 112 rejection could be overcome by limiting the terms "first amine protecting group," "second amine protecting group," and "weak leaving group" to those compounds or groups of compounds that are disclosed in the specification. For the first and second amine protecting groups, those compounds are 9-fluorenylmethyl carbamate, allyl carbamate, benzyl carbamate, substituted benzyl carbamate, t-butyl carbamate, 1-adamantyl carbamate, 2-nitrobenzenesulfonyl, triphenylmethyl, (4-methoxyphenyl)diphenylmethyl, and 9-phenylfluorenyl (see page 22, lines 14-18). For the weak leaving group, these compounds are short chain alkoxides, etiolates, azide, and sulfonamides (see page 22, lines 26-28).

With respect to the 35 USC 103 rejection of Claims 1-12 over Valli et al., "Synthesis and metabotropic glutamate receptor antagonist activity of N1-substituted analogs of 2R, 4R-4-aminopyrrolidine-2,4-dicarboxylic acid," Bioorganic & Medicinal Chemistry Letters 8 (1998), the Examiner requested that the Applicant express its arguments in writing so they can be more fully considered. In response, Applicant has provided its arguments herein under the section titled "35 USC 103 Rejections."

35 USC 112 Rejections

Claim 1 is rejected under 35 USC 112 because it is unclear which groups are encompassed by the terms "first amine protecting group," "second amine protecting group," and "weak leaving group."

Claim 1 has been amended to recite a first amine protecting group selected from the group consisting of 9-fluorenylmethyl carbamate, allyl carbamate, benzyl carbamate, substituted benzyl carbamate, t-butyl carbamate, 1-adamantyl carbamate, 2-nitrobenzenesulfonyl, triphenylmethyl, (4-methoxyphenyl)diphenylmethyl, and 9-phenylfluorenyl. Basis for this amended language is provided in the specification, e.g., at page 22, lines 14-18. Claim 1 has also been amended to recite a second amine protecting group selected from the group consisting of 9-fluorenylmethyl carbamate, allyl carbamate, benzyl carbamate, substituted benzyl carbamate, t-butyl carbamate, 1-adamantyl carbamate, 2-nitrobenzenesulfonyl, triphenylmethyl, (4-methoxyphenyl)diphenylmethyl, and 9-phenylfluorenyl. Basis for this amended language is provided in the specification, e.g., at page 22, lines 14-18. In addition, Claim 1 has been amended to recite a weak leaving protecting group selected from the group consisting of short chain alkoxides, thiolates, azide, and sulfonamides. Basis for this amended language is provided in the specification, e.g., at page 22, lines 26-28.

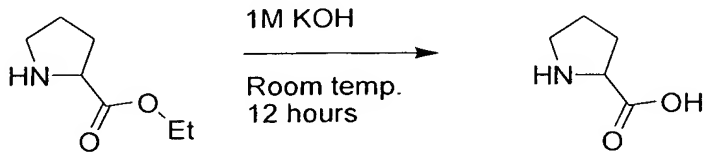
Because Claim 1 has been amended as the Examiner suggested in the July 15, 2005 interview (i.e., to recite specific compounds or groups of compounds that are disclosed in the specification), Applicant submits that amended Claim 1 meets the requirements of 35 USC 112. Applicant respectfully traverses the 35 USC 112 rejection with respect to Claim 1.

Claims 295-300 have been rejected under 35 USC 112 as failing to comply with the written description requirement. Claims 295-300 have been canceled.

35 USC 103 Rejections

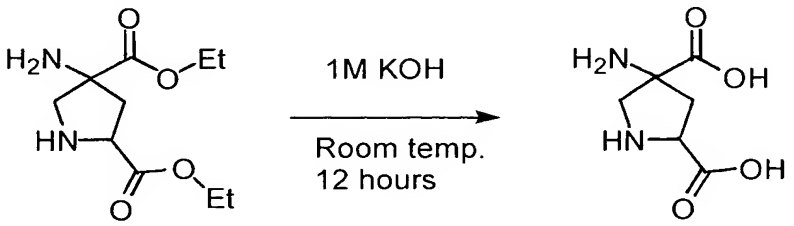
Claims 1-12 have been rejected under 35 USC 103 as being obvious in view of Valli et al., "Synthesis and metabotropic glutamate receptor antagonist activity of N1-substituted analogs of 2R, 4R-4-aminopyrrolidine-2,4-dicarboxylic acid," Bioorganic & Medicinal Chemistry Letters 8 (1998). According to the Office Action, the Valli et al. reference teaches the interchangeability of the acid and the ester group. Applicant respectfully traverses the 35 USC 103 rejection with respect to Claims 1 and 4-8. Claims 2-3 and 9-12 have been canceled.

It is a basic principle of organic chemistry that an acid and an ester are interchangeable. For example, a compound containing a single ethyl ester can be converted to a compound containing a single carboxylic acid using potassium hydroxide as follows:



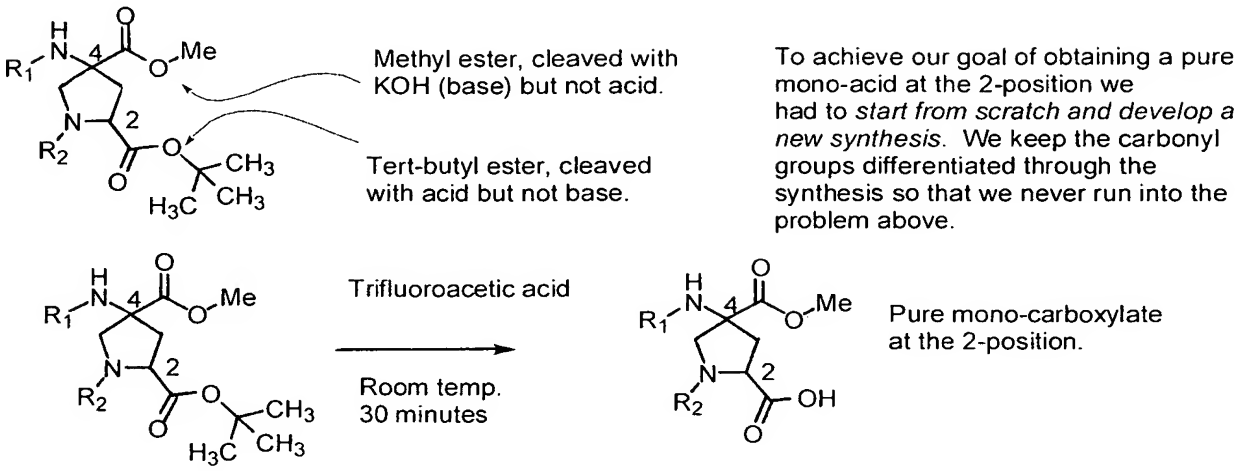
However, it is not obvious that on a molecule containing two esters, that a specific ester can be regioselectively hydrolyzed to become an acid while the other ester remains an ester. Moreover, it is not obvious that on a molecule containing two esters, a single ester can be regioselectively hydrolyzed to produce a desired mono-acid in high yield.

When a compound that contains two identical esters at the 2 and 4 positions (i.e., the compounds of Valli et al.) is subjected to a conventional process for interchanging an ester with an acid, both esters are rapidly converted into acids. As shown in the schematic below, KOH is not able to distinguish between the two identical esters.



KOH can't distinguish between the two ethyl esters. Both esters are attacked and a high yield of pure di-acid is obtained.

Conventional methods for interchanging an ester with an acid are not capable of achieving the compound recited in Claim 1, which is a high yield mono-acid, wherein the acid always occurs at the 2-position. The compound recited in Claim 1 was made using an entirely new synthetic route that deliberately maintains different protecting groups on the carbonyl groups at positions 2 and 4 in order to differentiate them. The following schematic describes this new synthetic route:



The compound recited in Claim 1 always contains a mono-carboxylic acid at the 2-position and an ester at the 4-position. It was synthesized using a temporary protecting group on the 2-carboxylate (here a tert-butyl ester) that was selectively removed with acid. Such selective removal of a particular ester is not possible using the compounds disclosed in Valli et al. because they contain identical esters. Thus, it would not have been obvious to a person skilled in the art to synthesize the compound of Claim 1 in view of Valli et al. The compound recited in Claim 1 would be an unexpected result to a person skilled in the art given the compounds disclosed in Valli et al. and their identical esters. Therefore, Claim 1 is not obvious in view of Valli et al., and the 35 USC 103 rejection is traversed with respect to Claim 1.

The 35 USC 103 rejection is also traversed with respect to dependent Claims 4-8 for the same reasons expressed hereinabove with respect to independent Claim 1. Because the compounds recited in Claims 4-8 always contain a mono-acid at the 2-position and an ester at the 4-position, these compounds would be non-obvious to a person skilled in the art given the compounds disclosed in Valli et al.

Summary

In view of the foregoing amendments and remarks, Claims 1 and 4-8 are believed to be in allowable form. Applicant respectfully requests allowance of the application.

In the event that any outstanding matters remain in connection with this application, the Examiner is invited to telephone the undersigned at 412-566-5941.

Respectfully submitted,

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